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THE SCOPE OF MODERN PHYSIOLOGY.

BY FREDERIC S. LEE.

(*Continued from page 388.*)

Three achievements of the present period have shown investigators how broad their science really is. First, the establishing of protoplasm as the physical basis of life, and of its substantial identity in plants and animals by Dujardin, Von Mohl, and Max Schultze, showed that the really fundamental problems of life and action had heretofore not been grasped; that the essential laws of protoplasmic activity apply to the whole organic world; and hence that any physiology which confines itself rigidly to either plants or animals to the exclusion of the other is a one-sided science. Second, the cell-theory of Schleiden and Schwann demonstrated that sooner or later many functions must be traced back to the cell, and that a cellular physiology is the key to a large proportion of the problems arising in the biological world. Third, the work of Darwin, based, as it was, upon physiological principles, showed that the action of the environment upon the individual and upon the species, as well as the action of the organism upon the environment, was an almost unworked field of the richest promise; that all physiology, in order to be complete, must be comparative; that there is an ontogenetic and a phylogenetic evolution of function; and that the physiological laws of heredity were yet to be discovered.

Let us examine these ideas briefly. The necessity of understanding the physiology of undifferentiated protoplasm is obvious, for there we find function in its simplest and most generic form. The phenomena of projection and retraction of pseudopodia in the Amoeba are doubtless the key to the complex processes of contraction and relaxation of striped muscular tissue. It is not at all improbable that the action of light upon the retina is a specialized derivative of the heliotropic phenomena of the simplest plants and animals. Four years ago, the well-known Oxford physiologist, Burdon Sanderson, wrote concerning the nature of the physiological inquiry, "The work of investigating the special functions, which, during the last two decades, has yielded such splendid results, is still proceeding, and every year new ground is being broken and new and fruitful lines of experimental inquiry are being opened up; but the further the physiologist advances in this work of analysis and differentiation, the more frequently does he find his attention arrested by deeper questions relating to the essential endowments of living matter, of which even the most highly differentiated functions of the animal or the plant organism are the outcome." Again, "No one who is awake to tendencies of thought and work in physiology, can fail to have observed that the best minds are directed with more concentration than ever before to those questions which relate to the elementary endowments of living matter, and that if they are still held in the background, it is rather because of the extreme difficulty of approaching them than from any want of appreciation of their importance. * * * * If we really understood them, they would furnish a key, not only to the phenomena of nutrition and growth, but even to those of reproduction and development. * * * * It is in the direction of elementary physiology, which means nothing more than the study of the endowments of living material, that the advance of the next twenty years will be made."

Regarding the need of a cellular physiology, it is only necessary to review our knowledge of any one of the complicated organs to perceive that aside from the principles, often chiefly mechanical, involved in the work of the organ as a whole, the essence of its activity lies in the activity of its component cells. The work of the muscle, *e. g.*, is the sum of the activities of its constituent physiologically similar fibres. A single gland cell illustrates the principles of secretion as well as, or even better than, a thousand grouped together into a compact gland. The complexity of brain operations is due to the complexity of brain structure, but the active agents are the comparatively simple nerve-cells. Huxley sets forth as the first three of the five chief ends of modern physiology: "Firstly, the ascertainment of the facts and conditions of cell-life in general. Secondly, in composite organisms, the analysis of the functions of organs into those of the cells of which they are composed. Thirdly, the explication of the processes by which this local cell-life is directly, or indirectly, controlled and brought into relation with the life of the rest of the cells which compose the organism." Now that the structure of protoplasm is fast becoming disentangled, a rational cell-physiology will be possible. In urging the need of investigating cell-function, I do not mean to imply that the cell is necessarily the ultimate unit, and that the organism is to be regarded as substantially a colony of physiologically independent cells. Much of the recent cytological work indicates that ere long the cell may be deposed from its hierarchical position.[1] Cellular interactions are to form an increasingly prominent place in the researches of cell-physiologists. But, whether or not we grant with many that the cell is of secondary significance, we must allow that, in many respects at least, it may be regarded as a physiological unit; and from this standpoint it demands investigation.

In these days of comparative science, it seems superfluous to urge the necessity of a comparative physiology. No one, who thinks seriously of the matter, will doubt that along with the morphological distinctions between different species, genera, orders, or classes, and even in cases where gross morphological distinctions are not apparent, there must be physiological differences. Beyond the obvious facts of simple observation, these are almost wholly uninvestigated. De Varigny, in his suggestive little book on Experimental Evolution, has collected a number of the known facts. In a garden in the south of France, were growing, side by side, a number of plants of the same species. There appeared to be no morphological differences between them, but some were indigenous to the soil in which they were growing, while others had been imported from the Canary Islands. When they were attacked by frost, all the Canary Island forms perished, while the French forms were untouched. There was evidently some obscure physiological difference between them. The two common European species of frogs, *Rana temporaria* and *Rana esculenta*, behave very differently toward certain drugs, as Schmiedeberg, Monnier, Vulpian, Harnack and Meyer, and others have shown. In *R. temporaria*, caffeine causes a decrease in excitability; in *R. esculenta* an increase; in *R. temporaria* pilocarpine causes paralysis; in *R. esculenta* tetanus. The venom of one snake is harmless for its own species, but poisonous for others. The spinal cord of the fish is differently endowed from that of the frog, though the differences have never been properly investigated. The muscle of the Insect is far removed functionally from that of the Crustacean, though how far remains to be discovered. I do not overlook the fact that already much excellent work upon the physiology of the Invertebrates and lower Vertebrates has been done, but too often such work has not been *comparative*. Fitness for the object of the research is the usual determinant of choice—and hence the frog has taught us most of our physiology of muscle. Sooner or later this must all be changed, the functional differences must be made known, and the exact position of each plant, each Invertebrate, and each Vertebrate, in the physiological series, together with the exact position of his organs and tissues and cells must be understood. For we must recognize the fact that function in any one species has *come to be*—an evolution of function is as much a reality as an evolution of form. The adult body and its organs, tissues and cells are the functional derivatives of the germ-cells—in the growth of the individual there has been a physiological ontogeny. So in the growth of the species there has been a progressive or retrogressive development of function; and one of the most attractive fields for our future work will be the tracing out of the phylogeny of function, now a practically unknown subject.[2] The difficulty of such an undertaking is great, for the rich palaeontological series is beyond the reach of the experimentalist. Yet this should be no bar to the systematic investigation of existing forms. Such a phylogeny will vary with each functional part (organ, tissue or cell); *e. g.*, if, in one genus, certain brain functions and certain secretory functions are always found, the presence of the same brain functions in another genus does not necessarily indicate the presence of the same secretory functions. Nor will the line of functional descent of a part necessarily coincide with the line of morphological descent of the organism. A natural system of classification is based and, justly so, on morphological considerations. In thus tracing out the genetic relationships of function, lie the attractiveness and the utility of the comparative method in physiology. And I venture to assert that, if all investigators would bear in mind the fact of an evolution of function, surprising advances would result in our knowledge of the working of adult organs.

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[1] Cf. Whitman, *Journal of Morphology*, VIII, No 3, August, 1893.

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[2] Cf. Dohrn, *Das Princip des Functionswechsel.*

What is it that makes an individual physiologically what he is? There are two agents—heredity and the environment. As to heredity, the active discussion now going on around Weismann as a centre, serves to show what a vast amount we do not know, on both the morphological and the physiological sides as regards the general phenomena of heredity and the nature and behaviour of the hereditary substance. No one recognizes this more fully than Weismann himself. He confesses that his own theory is far from complete; that its importance consists primarily in its suggestiveness; that the real solution of the problem lies in the future, and that facts are greatly needed. In this connection I may refer to the value of the work of Nussbaum, Gruber, Balbiani, Hofer, Korschelt, Verworn and others on the physiological relations of the nucleus and cytoplasm.

The mutual relations of the environment and the individual are almost as unknown as when Darwin first demonstrated their importance. In a few special lines they have been investigated. In his earthworm studies Darwin himself set an eminent example. The fact of the modification of the virulence of pathogenic bacteria by their treatment during growth is well known. Interesting results have been obtained regarding the action of salt-water on fresh-water animals, and *vice versa;* the action of salts on starch production in plants; the effect of depriving animals of apparently important salts, *e. g.*, fowls of carbonate of lime, and crabs of calcium chloride. Maupas's well-known studies on the influence of temperature on the determination of sex may be mentioned here, as well as those of Yung, Mrs. Treat, and others on the influence of foods. If an altered environment is capable of altering function—and we know this to be a fact—and if the altered function reacts upon structure—which is equally undoubted—then we find in these premises sufficient justification for searching after the facts concerning the nature and extent of environmental influence. The value of such researches lies not so much in the isolated results themselves, as in the fact that such results, when sufficiently numerous, will lead us directly not only to a better understanding of the internal physiology of organisms, but, what is of more general interest, to an understanding of the causes of variation, and thus to a better comprehension of the relations of species to one another. Too much cannot be said upon this phase of our subject. Whether the direct action of the environment is to be considered as a factor in organic evolution or not, the causes of variation must be investigated *experimentally*, and the physiological side of the work must not be neglected. Semper says, "Although the morphological section of animal biology[3] teaches with much probability that this species or that organ has undergone this or that course of modification in the animal series, and that in the process of modification it has passed through a whole series of various forms, still it is only physiological research that can elucidate the necessity for their existence by revealing their causative conditions."

One word regarding the relations of physiology and morphology. In the broad way in which I have outlined the former science, it may be charged that I have trespassed upon the morphological preserve. I do not deny the charge. It seems to me altogether unnecessary, undesirable and moreover impossible to draw a sharp line of distinction between the two sciences. With a common origin, mutual independence was, in time, necessary to the growth of each, yet this is in entire harmony with the fact that they have a common meeting-ground. In these days, as always, the morphologist must be something of a physiologist; the physiologist something of a morphologist. The current researches and discussions on evolution, heredity, and other fundamental questions make this constantly more evident. Like zoology and botany, each has its special field of labor, its special methods, and its special problems; but the fields are constantly overlapping, the one learns methods from the other, and the ultimate problems of both are the same.

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[3] He might justly have omitted the word "animal."

Let us now draw together the main lines of our thesis. I prefer to conceive of physiology as the science of the dynamics of living matter. Its tasks for the future seem to comprise the following classes of investigations.

First, the functions of adult organs, tissues and cells in plants, Invertebrates and Vertebrates. The greatest interest at present appears to center about the phenomena of heredity, the central nervous system, and general cell physiology. Second, the ontogeny of functions, or embryological physiology. Third, the phylogeny of functions. Fourth, the physiology of organisms, comprising the mutual relations of organisms to each other and to their environment.

It would be superfluous here to discriminate between the opportunities for research offered in these four classes of problems. Each covers a wide field of rich promise. Each is largely worked—in reality, as we have shown, research in the past has been confined almost wholly to the first group. Each will lead the investigator to fundamental problems.

In considering these tasks it will be perceived that I have viewed the organism in two aspects, in its internal and its external relations. The problems of the first three groups may be regarded as belonging to *internal physiology*, those of the fourth to *external physiology*. Nearly twenty-five years ago, Haeckel made a similar division into *Conservations-* and *Relations-Physiologie*.[4] Such a classification is convenient and valuable. But it must be remembered that it is artificial, and must not be taken as indicating a fundamental distinction between two sciences. The two are departments of the one science, physiology, and pass the one into the other. For a fact that becomes the more striking, the longer one studies the dynamics of living matter, is the utter impossibility of drawing a sharp line between the internal and the external. The functional organism is constantly acted upon by the environment, and is incapable of existence apart from it. But the functional organism is but the *ensemble* of the functional parts, and the parts are linked functionally together, constantly acting and reacting upon each other and modifying each other's work. It follows that the innermost portions cannot free themselves from environmental influence, and the attempt at an essential separation of internal from external physiology is in vain. Nor is such an attempt justified any the more by methods of investigation. For he who studies the action of light upon the retina, is thereby fitted to investigate the heliotropic phenomena of the organism; and he who is familiar with methods by which the effect of salts or temperature on the organs is tested, is most capable of testing the influence of the composition and the temperature of the surrounding water upon aquatic animals and plants. I speak of this the more especially because of the fact that, since the completion of the greater portion of this paper, the able address of Professor Burdon Sanderson, as President of the British Association for the Advancement of Science, has appeared.[5] In an interesting manner Professor Sanderson reviews the aspects of physiology since the time of Müller. He says, "The distinction * * * * between the internal and external relations of plants and animals has, of course, always existed, but has only lately come into such prominence that it divides biologists more or less completely into two camps—on the one hand, those who make it their aim to investigate the actions of the organism and its parts by the accepted methods of physics and chemistry, carrying this investigation as far as the conditions under which each process manifests itself will permit; on the other, those who interest themselves rather in considering the place which each organism occupies, and the part which it plays in the economy of nature. It is apparent that the two lines of inquiry, although they equally relate to what the organism *does*, rather than to what it *is*, and therefore both have equal right to be included in the one great science of life, or biology, yet lead in directions which are scarcely even parallel." Giving then a somewhat misleading interpretation of Haeckel's ideas above referred to, Professor Sanderson proceeds to divide Biology into three parts, Morphology, Physiology, which deals with the "internal relations of the organism," and Oecology (a term borrowed from Haeckel) "which concerns itself with the external relations of plants and animals to each other, and to the past and present conditions of their existence." In another place, Professor Sanderson says, "No seriously-minded person, however, doubts that organized nature, as it now presents itself to us, has become what it is by a process of gradual perfecting or advancement, brought about by the elimination of those organisms, which failed to obey the fundamental principle of adaptation, which Treviranus indicated. Each step, therefore, in this evolution, is a reaction to external influences, the motive of which is essentially the same as that by which, from moment to moment, the organism governs itself."

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[4] *Jenaische Zeitschrift*, V, 1870.

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[5] *Nature*, September 14, 1893.

I realize how presumptous it appears in me to differ from or attempt to criticise the views of one who occupies so deserved a place among the foremost physiologists of to-day. Yet I cannot repress the thought that the author of the Nottingham address viewed his subject more in the waning light of a day that is ending than in the brightening beams of a coming dawn. If each "step * * * * in this evolution is a reaction to external influences," why should not the student of the "steps" study also the origin and causation of those steps? I think he would justly be open to the charge of narrowness if he did not do it. And, moreover, as I have indicated above, I believe not only that he of all is best fitted, but that a rational view of his science forces him to do it. The progress of a scientific physiology has been greatly retarded by its followers confining themselves too exclusively to "the internal relations of the organism." Not the least of the retarding consequences is the fact that thereby the science loses much of its attractiveness. Just as anatomy, illumined and vivified by the theory of evolution, and broadened by the incorporation of embryology and paleontology, became the science of morphology, so I believe that physiology is destined to undergo, and is undergoing, a similar vivifying and broadening process, and is to become the science of vital phenomena, wherever and however they may be exhibited.